(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
9 October 2003 (09.10.2003)

PCT

(10) International Publication Number
WO 03/082322 A1

(51) International Patent Classification[7]: A61K 38/43, 38/18, 38/19, 38/00, A61P 29/00, 35/00, 37/00

(21) International Application Number: PCT/AU03/00388

(22) International Filing Date: 28 March 2003 (28.03.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

PS 1448	28 March 2002 (28.03.2002)	AU
PS 1538	5 April 2002 (05.04.2002)	AU
PS 1621	8 April 2002 (08.04.2002)	AU
2002951668	19 September 2002 (19.09.2002)	AU
2003900230	21 January 2003 (21.01.2003)	AU

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/082322 A1

(54) Title: A METHOD OF MODULATING CELLULAR ACTIVITY

(57) Abstract: The present invention relates generally to a method of modulating cellular activity and to agents for use therein. More particularly, the present invention provides a method of modulating cellular activity by modulating phosphorylation of sphingosine kinase and, thereby, its activation. In a related aspect, the present invention provides a method of modulating sphingosine kinase functional activity via modulation of its phosphorylation and agents for use therein. The present invention still further extends to sphingosine kinase variants and to functional derivatives, homologues or analogues, chemical equivalents and mimetics thereof exhibiting reduced and/or ablated capacity to undergo phosphorylation. The method and molecules of the present invention are useful, *inter alia*, in the treatment and/or prophylaxis of conditions characterised by aberrant, unwanted or otherwise inappropriate cellular and/or sphingosine kinase functional activity. The present invention is further directed to methods for identifying and/or designing agents capable of modulating sphingosine kinase phosphorylation.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU03/00388

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. [7]: A61K 38/43, A61K 38/18, A61K 38/19, A61K 38/00, A61P 29/00, A61P 35/00. A61P 37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Refer to electronic database consulted below

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
DWPI and MEDLINE. Keywords: sphingosine kinase or sphk or sph kinase, proline directed kinase, ERK, CDK2, TNF, U0126 or PD98059

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/12533 A (MEDVET SCIENCE PTY.LTD) 18 March 1999 Whole document	1-45
X	WO 01/85953 A (MEDVET SCIENCE PTY.LTD) 15 NOVEMBER 2001 Whole document	1-45
X	BLAUKAT, A et al. Activation of sphingosine kinase by the bradykinin B_2 receptor and its implication in regulation of the ERK/MAP kinase pathway. Biol. Chem. January 2001, vol. 382, pages 135-139	1-9, 12-20, 28-36, 44 and 45

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
	29 MAY 2003

Name and mailing address of the ISA/AU	Authorized officer
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU03/00388

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MACHWATE, M et al. Sphingosine kinase mediates cyclic AMP suppression of apoptosis in rat periosteal cells. Molecular Pharm. 1998, vol. 54, pages 70-77 Abstract, Col. 2, page 76 onwards	1-45
X	CUVILLIER, O et al. Spgingosine-1-phopshate antagonizes apoptosis of human luekemia cells by inhibiting release of cytochrome *c* and Smac/DIABLO from mitochondria. Blood, November 2001, Vol. 98(9), pages 2828-2836 Abstract, Col. 2, lines 24 onwards	1-45
X,P	Johnson, KR, et al. PKC-dependent activation of sphingosine kinase 1 and translocation to the plasma membrane. J. Biol. Chem. September 2002, vol. 277 (38), pages 35257-35262	1-45
X,P	MACEYKA, M et al. Sphingosine kinase, sphingosine-1-phosphate, and apoptosis. Biochimica et Biophysica Acta, 2002, Vol. 1585, pages 193-201 Whole document	1-47
X,P	WO 02/098458 A (MEDVET SCIENCE PTY.LTD) 12 December 2002 Page 15, paragraph 2 Pages 19 and 20, and claims 1, 2, 9, 10, 19, 20	1-45

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/AU03/00388

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
WO	99/12533	EP	1011654	JP	2001515857T	CA	23002838
WO	02/098458						
WO	01/85953	AU	56001/01				

END OF ANNEX